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This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

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Additional inventors are being named on the ______ separately numbered sheets attached hereto

TITLE OF THE INVENTION (500 characters max)

Optical Measurement of Hematocrit

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USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

Optical Measurement of Hematocrit
Gregory Crawford, Ph.D., and Gregory Jay, M.D.

C. PROJECT DESCRIPTION

This proposal involves the fusion of engineering and core medical expertise to develop novel spectroscopic devices. The project is based on the innovative integration of modern materials and electro-optic technology to create electrically switchable color devices for the fast and non-invasive measurement of hemoglobin, useful in the detection of anemia and determining the age of bruises. The proposed device can have tremendous impact on the medical community and society while advancing the engineering knowledge base. This device would provide a general health care tool to measure hemoglobin concentrations in the body, which are an early indicator of serious diseases, be a potential home health care technology for the chronically ill and aging, be a tool to enable physicians to accurately age bruises for a variety of reasons, including domestic and child abuse cases which have dramatic consequences, and have the potential to reduce health care costs. The ability to non-invasively measure hemoglobin concentrations by imaging the palpebral conjunctiva and to age bruises on the human body may be seemingly disparate applications, but there is tremendous synergy between the two since they deal with determining the concentrations of hemoglobin and hemoglobin breakdown. Although we do not focus on other applications in this proposal, we believe the technology developed under this award will be equally attractive to many other areas and industries, including dermatology, ophthalmology, dentistry, emergency medicine, and forensic medicine to name a few.

C.1 Motivation

C.1.1 Anemia

Anemia is often perceived by the general population to be a minor medical condition; however this is a very naïve attitude and certainly an opinion adamantly opposed to by physicians and other health care professionals. According to the *World Health Organization*, anemia is the single largest global illness adversely affecting mortality and worker capacity, and The *United States Department of Health & Human Services* deemed anemia a significant public health concern [*NAAC, 2003*]. Of the 16 million people estimated to have anemia in the United States, 78% of them go undiagnosed. In developing 3rd world countries where nutritional inadequacies and infectious disease are more prevalent, sadly the situation is estimated to be even worse, severely hindering children to reach their full genetically determined potential [*Ulijaszek, 1994; Verhoef, et al., 2002*].

Anemia is the lack of healthy red blood cells in an individual's body which leads to an oxygen deficiency in the body's tissues and organ systems. Medically, anemia is defined by the *World Health Organization* (*WHO*) as a hemoglobin concentration below 12 g/dL for females and below 13 g/dL for males [*WHO, 1968*]. Anemia is well known to the general population to influence physical function through fatigue and weakness. Anemia also decreases myocardial function and increases peripheral arterial vasodilation and activation of the sympathetic and reninangiotensin-aldosterone system, which strongly influences the initiation or progression of diseases such as heart failure and renal failure [*Toto*, 2003; *Pereira and Sarnak*, 2003; *Silverberg, et al., 2001; Anand, et al, 1993; Goldstein, et al., 1996; Georgieva and Georgieva, 1997*]. Approximately the same number of people have anemia in the United States as have diabetes. In addition, anemia affects patients with other diseases: at least 33% of all cancer patients, an estimated 65%-95% of all HIV/AIDS patients, and 70% of all rheumatoid arthritis patients.

Age related disability and loss in physical function are mounting public health concerns [*Guralnik, et al, 1996*]. Loss of physical function endangers the quality of life and independence of many older adults, and has significant social and economic repercussions [*Fried, et al., 2001*]. The prevalence of anemia increases with age and averages about 13% in person's ≥70 years of age (*Salive, et al., 1992*). A majority of the anemia in aging adults signifies diseases such as cancer and infectious ailments or are due to iron deficiency or malnutrition [*Joosten, et al., 1992; Ania, et al., 1997; Mitrache, et al., 2001*]. However, for 20% of cases in elderly it is not possible to attribute anemia to such factors. Recent studies report that anemia in aging adults is an independent risk factor for decline in physical performance [*Penninx et al.*, 2003] and is associated with higher mortality risks [*Izaks, et al., 1999*].

The reason anemia is under diagnosed is two fold. To determine whether or not a patient is anemic, th physician has two options: (1) a visual inspection of the palpebral conjunctiva as shown in Figure 1(a) or (2) a cell blood count (CBC) test. The visual inspection of the conjunctiva by a physician is at best 70% accurate and dependent on the physician's experience and training, and it has been shown that

physicians today are less accurate than those of the past [*Hung, et al., 2000*]. The CBC test is very accurate, but it is painful to the patient, expensive to perform, it takes time to get the analysis back from the laboratory, and it is oft n not part of a routine physical exam. There is a need for a n w tool that can m asure hemoglobin accurately, quickly and inexpensively, which can be as common and useful to health care professionals as a stethoscope and sphygmomanometer. Because of the need to measure heomoglobin in a more effective way, there have been a number of device concepts disclosed in the patent literature, such as retinal imaging [*Rice, et al., 2001*], blood oxygenation monitoring [*Benni, 2002; Diaconu, et al., 2000*], in-vivo imaging of blood [*Groner and Nadeau, 2000*], blood analyzer [*Ishihara, et al., 1998*], photoplethysmography [*Carim, et al., 1998; Aldrich, 2000*], image processing of blood vessels [*Winkelman, 1991*]. None of these solutions have been embraced by health care professionals predominately because of inconvenience and inaccuracies.

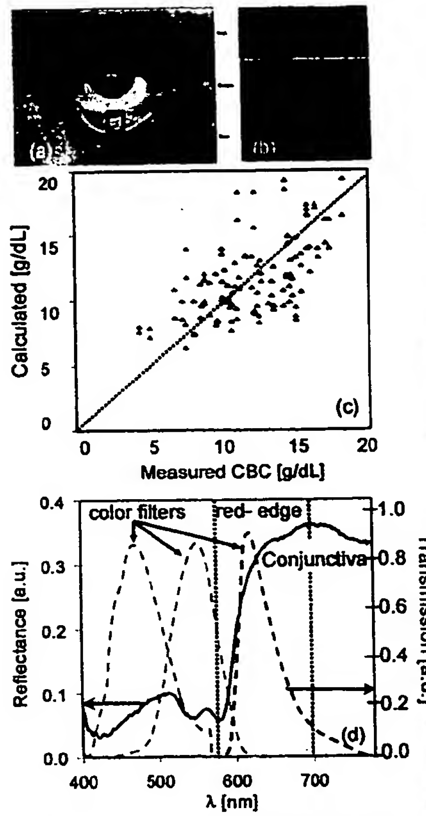

Figure 1: *A photograph of a human conjunctiva (a), photographs of the conjunctiva as viewed with red, green and blue filters (b), preliminary results for predicting hemoglobin using a PDA (c), and spectra of a human conjunctiva with superimpose transmission spectra of color filters (d).*

A device that can quickly, accurately, and portably measure hemoglobin has many health care applications, such as in routine physical examinations, in emergency rooms, for emergency rescue professionals, during surgery for in-situ measurement of hemoglobin (bleeding), home health care for the chronically ill and aging population, in developing countries where anemia is prevalent, medical facilities are scarce, resources are limited, and medicine is practiced in the field, military medical units, mass casualty situations and triage units, and specialist who deal with anemia on a regular basis (oncology, pediatrics, obstetrics, gynecology, anesthesiology, infectious disease, gastroenterology, cardiology, nephrology, geriatrics, and urology).

C.1.2 Bruising

Internists and pediatricians are often asked for an opinion on the age of externally visible contusions (*e.g.* bruises) for many reasons (*e.g.* child protection cases or legal proceedings to attempt to identify perpetrators and to determine whether multiple episodes have occurred). In many circumstances, they are expected to give an opinion on whether or not the bruising pattern is consistent with abuse. Sadly enough, physical abuse or inflicted trauma is one of the most common types of child maltreatment observed by physicians [*Schmidtt, 1997*].

Child welfare and criminal justice systems make judgments of great consequence based on physician opinions regarding clinical evidence. A recent study has shown that physicians' estimates of bruise age is highly inaccurate, and appear to be no better than chance alone [*Bariciak, et al., 2003*]. Even when a bruised area was examined directly, it was still difficult for physicians, independent of training and clinical experience, to reliably estimate the age of a bruise [*Bariciak, et al., 2003*]. The fact that emergency physicians, pediatricians, and front line social and health care workers who assess injured tissue on a regular basis have inadequate accuracy in estimating the age of a bruise, underscores the need for a device that can accurately and quantitatively measure the age of bruises. Although there have been basic studies on spectrophotometrically evaluating bruising with conventional spectroscopic equipment [*Bohnert, 2000*] and new models to predict skin reflectance spectra [*Meglinski and Matcher, 2003*], there is no instrument available for physicians to ag bruis s. Since there is so much at stake in assessing the nature and age of bruises, there is a compelling need for an accurate device to assess bruises.

C.2 Preliminary Results-Proof of Conc pt

C.2.1 Hemoglobin Measurements and the Conjunctiva

The conjunctiva is a mucous membrane whose surface is composed of nonkeratinizing squamous epithelium, intermixed with globlet cells (mucus), Langerhans' cells, and occasional dendritic melanocytes. The palpebral conjunctiva, shown in Figure 1(a), covers the posterior surface of the eyelid. Since the conjunctiva is transparent and blood vessels are close to the surface, a physician can visually examine the palpebral conjunctiva, and based on its redness, he/she can make a judgment on whether the patient is anemic or not (low levels of hemoglobin). This is a common procedure in any physical exam [*Hung, et al., 2000*].

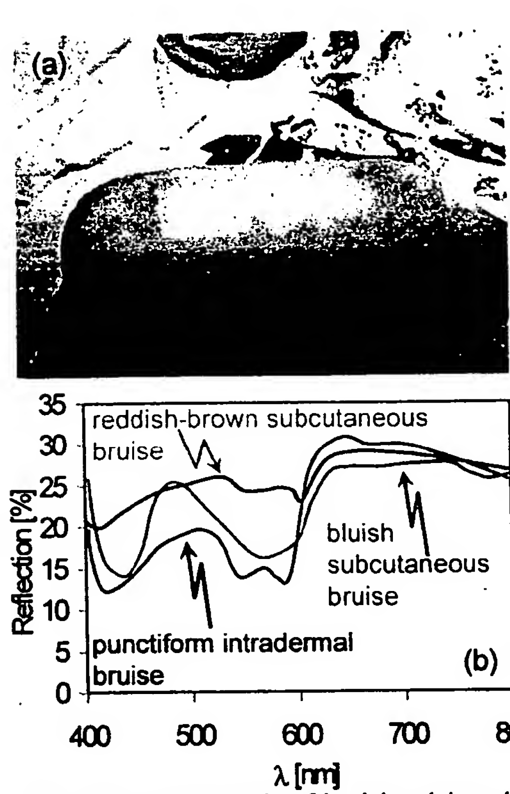

***Figure 2:** An example of bruising (a) and the spectral signatures associated with different types and ages of bruises (b) [data in (b) adapted from Bohnert, et al, 2000].*

Jay has recently performed a study at *Rhode Island Hospital* to see if the hemoglobin could be accurately determined from digital pictures (taken with a PDA) of the patients palpebral conjunctiva as shown in Figure 1(a). The sample set of patients included 63 emergency department patients and excluded patients with active bleeding, oxygen saturation <90%, and serum bilirubin concentrations over 3.0 mg/dL. An empirical algorithm was constructed using the red, green and blue images of the conjunctiva shown in Figure 1(b) to correlate the results of the image to actual CBC blood tests used to determine the hemoglobin concentration in the blood. The correlation is certainly present, as can be observed from Figure 1(c), but the largest problem is significant scatter in the data with respect to the 1:1 correlation line. The inaccuracy in this approach is evident from the spectra of an actual conjunctiva shown in Figure 1(d). The reflection spectrum of the conjunctiva, shown in Figure 1(d), is dominant in the red spectral region (denoted as red-edge). The transmission spectra of the color filters of a typical digital camera are overlaid on the conjunctiva spectrum. The spectral resolution of this approach is very low since the conjunctiva is red and we are looking for subtle differences in the redness of the conjunctiva to accurately correlate it to the hemoglobin level of the patient. It is clear from Figure 1(d) that the blue and green filters are not providing any spectral information, while the red does have significant overlap with the conjunctiva spectrum. However, using this approach, the correlation is substantially based on intensity of the red color channel only. This initial study does show the underlying principle of our concept. However, to significantly improve on the accuracy, we propose to reconstruct the spectrum of the conjunctiva using a spectral imaging device based on electrically switchable color filter technology.

C.2.2 Spectroscopy of Bruising

Visible contusions or bruises of the skin are typical consequences of blunt impact trauma. Bruises develop after the rupture of blood vessels do to compressive or shearing forces imposed on the body. Bruises are characterized as either subcutaneous or intracutaneous depending on the tissue layer that is affected [*Bohnert, et al., 2000*]. A subcutaneous bruise appears at the site of impact or indirectly by local expansion or shifting of the hemorrhage. After a time interval of hours to days, hemorrhages that are originally localized deep in the tissue layers can extend toward the surface. The bruise can change color over the course of its life, from blue to green to y llow in the course of days. Intracutan ous bruises are usually punctiform and they are gen rally identified by their bright red color. Th y are usually the result of a significant blunt impact. In fact, their shap can b the negative image of the impact instrument. When this skin is forced into channel or profile, the blood is forced into those sections of th skin not exposed to

pressure with hemorrhages occurring as a result of vascular ruptures in the dermis. The bruise appearance changes over time due to hemoglobin breakdown and diffusion processes. There have been many studies on bruising. And perhaps more importantly, on how to date bruises and distinguish abuse from accidental bruising [*Bariciak, et al., 2003; Dunstan, et al., 2002; Carpender, 1999*],.

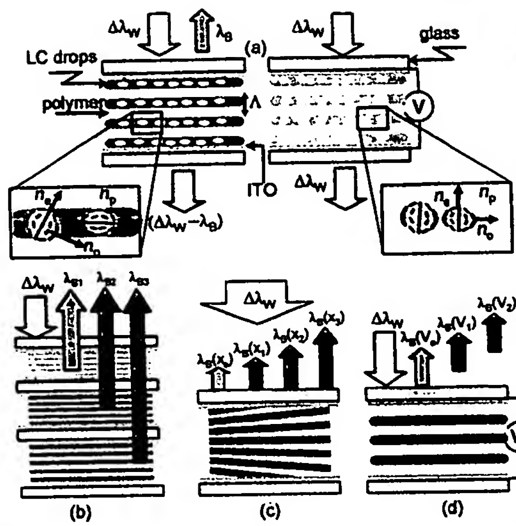

Figure 3: Basic operation of an H-PDLC (a), and three modes of operation including stacking (b), chirping (c) and electricallv tenabilitv.

Duffy is an expert in bruising; in particular, in child abuse cases. Figure 2 (a) shows an example of a photograph of a bruise taken at *Rhode Island Hospital* and Figure 2(b) demonstrates the radical differences in spectral signature of subcutaneous and of punctiform intracutaneous bruises. The age of the bruise is also observed in the spectrum; for example, see the difference in Figure 2(b) between the spectral signature of the young subcutaneous (bluish bruise) and the mature one (reddish-brown). There is compelling evidence that the color impression of a bruise or its spectral signature can help accurately pinpoint the age of a bruise and that hemoglobin degradation is one indicator of the age of a bruise [*Bohnert, 2000*]. Although there are a few recent studies and models of the spectroscopic assessment of skin to help diagnose various skin diseases [*Meglinski and Matcher, 2003; Wallace, et al., 2000*], there is no device or algorithm that can accurately predict the age of bruises. There is very little research in this area and clinical bruising assessments are routinely made by physicians without the support of evidence based standards. There is currently no objective standard or device for assessing bruises in living patients and therefore there is a compelling need for such an instrument. We propose to reconstruct the spectrum of the bruise using a spectral imaging device based on electrically switchable color filter technology, which can measure the degree of hemoglobin breakdown in the traumatized area.

C.3 Engineering and Technology Impetus

We proposed to push forward our unique science and engineering knowledge base at *Brown University* to create a biophotonic device that can non-invasively measure hemoglobin concentrations in patients by capturing an image of their conjunctiva and to accurately measure the age of a bruise through spectral analysis. We chose these two application areas since Jay and Duffy provide core medical expertise in these areas and there is significant cross-fertilization and synergy between the two applications to justify our parallel application approach. The underlying scientific and engineering principle is to use electrically switchable color filter technology based on liquid crystals to create an optical device that can perform spectrometry and spectral imaging fucntions. Crawford is an expert in liquid crystals and optics and will investigate and screen several approaches. There are three technologies that will be discussed in this section, based on holographically formed polymer dispersed liquid crystals (H-PDLCs), cholesteric liquid crystals (CLCs) and ferroelectric liquid crystals (FLCs). The strategy is to accelerate the knowledge base of these three technologies for the chosen applications during the first year of the program and choose the appropriate technology that ultimately satisfies the application specifications to develop further.

C.3.1 Holographically Formed Polymer Dispersed Liquid Crystals

Holographic polymer dispersed liquid crystals are created by a simple one-step fabrication process, where a homogeneous mixture of photosensitive prepolymer and nematic liquid crystal is exposed to an interference pattern process [*Bowley and Crawford, 2000*]. In the bright regions of the interference pattern, the polymerization occurs more rapidly than in the dark regions, thereby forcing out the non-reactive liquid crystal to th dark regions. This counter-diffusion process quickly creates a stratified compositional profil (liquid crystal droplets and polymer rich layers) that is ultimately locked-in by the photo-polymerization process. The grating pitch is given by $\Lambda=\lambda_f/2<n>\sin\Theta$, where λ_f is the wavelength of the exposing laser beams, <n> is the average index of refracti n of the film, and 2Θ is the angle between

the exposure beams inside the sample. Since the liquid crystal typically has an average index of refraction, n_{LC}, that is larger than that of the polymer, n_P, a spatial perturbation in the index of refraction exists. Crawford's laboratory is recognized as a academic leader in this field, having a number of publications and patents. Because of the laboratory's visibility in this area, General Motors recently donated the original H-DPLC patent to *Brown University* to complement and strengthen their intellectual property portfolio in this area [*Vaz, et al., 1992*].

One embodiment of H-PDLC materials is a switchable mirror shown in Figure 3, where the holographic planes are parallel to the glass substrates. In order to enable electrical switching, a transparent conductor is deposited on the substrates, most commonly, indium-tin-oxide (ITO). In the absence of an applied voltage (Figure 3(a)), a refractive index modulation exists between the liquid crystal rich planes (shown as droplets) and the pure polymer planes. The average index of refraction of the liquid crystal rich layers, n_{LC}, is some combination of the ordinary, n_o, and the extraordinary, n_e, index of refraction of the liquid crystal [often estimated as $n_{LC}^2 \approx (n_e^2+2n_o^2)/3$)]. When the film is illuminated with a broadband white-light source, denoted as $\Delta\lambda_W$, a narrow reflection band centered at λ_B is rejected with reflectivites >50% and peak widths, $\Delta\lambda_{FWHM}$, in the 15-30 nm range depending on the birefringence of the liquid crystal, index of refraction of the polymer, and sample thickness. Since liquid crystal molecules possess a positive dielectric anisotropy ($\Delta\varepsilon$>0), they align parallel to the applied electric field when an external voltage is applied as shown in Figure 3(b). In the aligned state, the ordinary refractive index of the liquid crystal, n_o, matches that of the polymer, n_p, the index modulation vanishes. The film becomes transparent to all wavelengths as shown in Figure 3 (a). The switching voltages tend to be on the order of 70-100 volts since the liquid crystal is highly constricted by the holographic planes of dimensions 170-200 nm for visible reflections; however, the dynamic response times can be very attractive (in some cases <100 μs) [*Crawford, 2003*]. H-PDLCs can be engineered to reflect ultraviolet, visible, and near infrared wavelengths [*Crawford, 2003*].

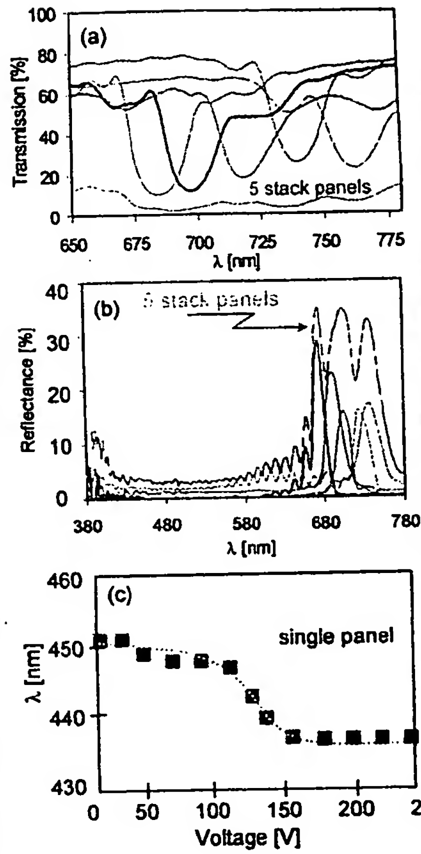

***Figure 4:** A H-PDLC stacked device consisting of 5 panels in transmission (a) and in reflection (b), and a single variable reflecting H-PDLC (c).*

There are several modes of operation. Figure 3(b) shows a three panel stack, with broad band incident white light, $\Delta\lambda_W$, and three reflection bands λ_{B1}, λ_{B2}, and λ_{B3}, whose peak wavelength is dictated by Bragg's law, $\lambda_B=2d\langle n\rangle$ for normally incident light, where *d* is the plane thickness. This is a very attractive approach to create a spectroscopic or spectral imaging element since the given Bragg reflection band can be turned on or off electrically. Figure 4(a) shows an actual five stack panel device in transmission and Figure 4(b) shows the five-stack device in reflection (this is a proof of concept data and is not targeted at the conjunctiva application 580 nm -680 nm). There are also other modes of operation, including chirping, shown in Figure 3(c), where the reflected Bragg peak, $\lambda(x_i)$, is a function of the spatial position on the sample, x. A chirped H-PDLC is obtained by creating the interference pattern with diverging beams thereby spatially changing the thickness of the Bragg planes, *d*, within the sample as a function of position [Kaiser, et al., 2004]. The final mode of operation is shown in Figure 3(d) and the data is shown in Figure 4(c) for the blue spectral range. The peak wavelength, $\lambda(V_i)$, can actually be tuned as a function of applied voltage V. We have demonstrated a 12 nm tunability range in the blue spectral region, with 1 nm of tunable peak resolution. Assuming linearity in the transition region in Figure 4(c), the tunability/resolution metric is $\Delta V/\Delta\lambda \sim$ 4 V/nm for the peak maximum.

We will pursue a hybrid approach with this technology to achieve the highest resolution for our spectroscopic application, using the stacking technique (Figures 3(b) & 4(b)) and the electrical tunablity function (Figures 3(d) & 4(c)). Chirping is an option and we can expect a 100-150 nm range over a 5 mm spot size; however, this approach would only be valid if we focus on conventional spectrometry where the imaged area is assumed to be uniform and abandon spectral imaging options. Therefore we will pursue the hybrid approach for the conjunctiva application focusing on creating a five stack panel, with each panel having 20 nm of tunability, to cover the red-edge of the conjunctiva spectral region between 580 and 680 nm. Using our model developed for the tunable device shown in Figure 3(d), we expect to achieve a λ_{shift}=20 nm spectral tunability range based on the following equation, $\lambda_{shift}=\lambda_B(\Delta/2<n>)$, assuming an index modulation Δ=0.1, a starting wavelength of λ_B=20 nm, and an average index of refraction $<n>$=1.5 [*Bowley, et al., 2000*]. For the bruising application, we believe that this technology may not be appropriate since it would require spectral coverage over the entire visible spectrum, which would require ~20 stacked H-PDLC panels. Due to the unwanted incoherent scattering observed in the transmission mode data presented in Figure 4(a), which is due to the scattering of the droplets and more noticeable in the blue spectral region [*Li, et al., 2004*], we believe that the reflection mode is the natural choice to achieve our application goals. We believe it is a challenging but not insurmountable engineering problem to create a voltage controllable stack. We have all of the expertise and infrastructure at *Brown University*.

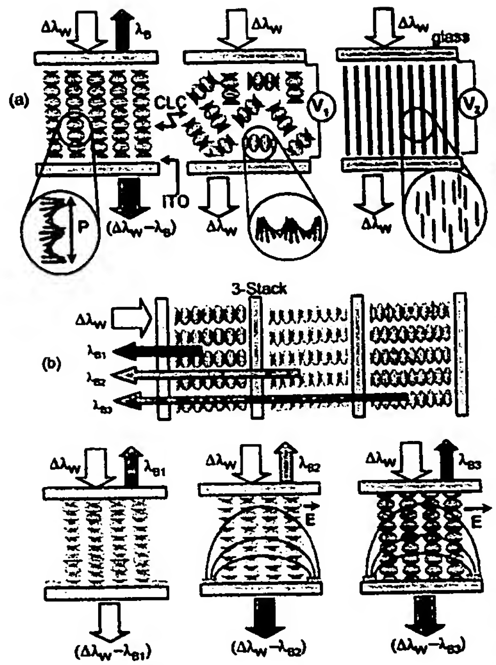

***Figure 5:** A mode of operation for the CLC panel with the planar (left), focal conic (middle) and homeotropic (right) states (a), a three stack CLC device to achieve full spectral coverage, and an IPS mode to achieve tunability (c).*

C.3.2 Cholesteric Liquid Crystals

Cholesteric liquid crystals (CLC) exhibit long range orientational order analogous to conventional nematic liquid crystals, except that the molecules are chiral [*Blinoff and Chigrinov, 1994*]. As a consequence, the structure acquires a spontaneous twist about a helical axis normal to the director (average direction of liquid crystal molecules). The degree of twist of the phase is characterized by the cholesteric pitch, P. The twist may be right- or left-handed depending on the molecular chirality.. These materials are being developed for flat panel display applications [*Yang, et al., 1996; Doane, et al., 2004*]. The operation of CLC device is shown in Figure 5(a, left). In the zero voltage state, the molecules are aligned in the planar configuration, and since the structure is periodic, they can reflect a bandwidth centered at λ_B, which is dictated by Bragg's law ($\lambda_B=<n>P$ for normal incidence). Upon application of an applied voltage (V_1~10-15 volts for a 5 μm sample), a positive dielectric anisotropy material ($\Delta\varepsilon>0$) transforms to a focal conic state, which is characterized by a random distribution of helical pitches as shown in Figure 5(b, middle). This state is transparent in the visible region and remains that way even after the voltage is removed (i.e. this device possesses bistable memory since the focal conic state can remain indefinitely even after the field is removed). Upon application of a higher voltage (V_2~25-30 volts), the material transforms to the hometropic state (aligned) as shown in Figure 5(a, right). When the voltage is abruptly removed, the homeotropic state transforms back to the reflective planar state. The chiral pitch can be engineered (by mixing in different concentrations of chiral components) to reflect in the ultraviolet, visible and near infrared. The switching time is slower than other materials discussed in this section, on the order of 30-50 ms depending on the mode.

There are two principle modes of operation to achieve full spectral coverage in the visible. Figure 5(b) shows a three-stack of CLC panels that reflect red, green and blue. The data for a three panel stack is

presented in Figure 6 (a) in the transmission mode and Figure 6(b) for the reflection mode. Since CLC are intrinsically right handed or left handed because of their chirality, they can reflect only right handed or left handed circularly polarized light (ideally 50% efficiency at the Bragg wavelength). In order to alleviate this problem, we were able to get more efficiency out of our panels as demonstrated in Figure 6(a) and (b) (exceeding 80%). The panels that reflected red, green and blue in Figure 6 were actually panel pairs, so we actually had six panels in the stack. We integrated a quarter-wave plate between two identically reflecting panels to achieve a much higher efficiency as demonstrated in Figure 6(a) and (b). One can also stack a left handed panel and a right handed panel with the same λ_B to achieve the same outcome. The CLC in-plane switching (IPS) mode is shown in Figure 6(c) (field direction parallel to the substrates, orthogonal to how it was applied in (a) and (b)). We have recently developed this IPS mode and were able to use one panel to span nearly the entire visible spectral range as shown in Figure 6(c). As an in-plane voltage is applied perpendicular to the pitch axis of the CLC, the pitch elongates and the reflection red-shifts. We were able to electrically tune the reflection band from 450 nm to 700 nm. Assuming linearity in the transition region, the tunability/resolution metric is $\Delta V/\Delta\lambda \sim 0.15$ V/nm for the peak maximum.

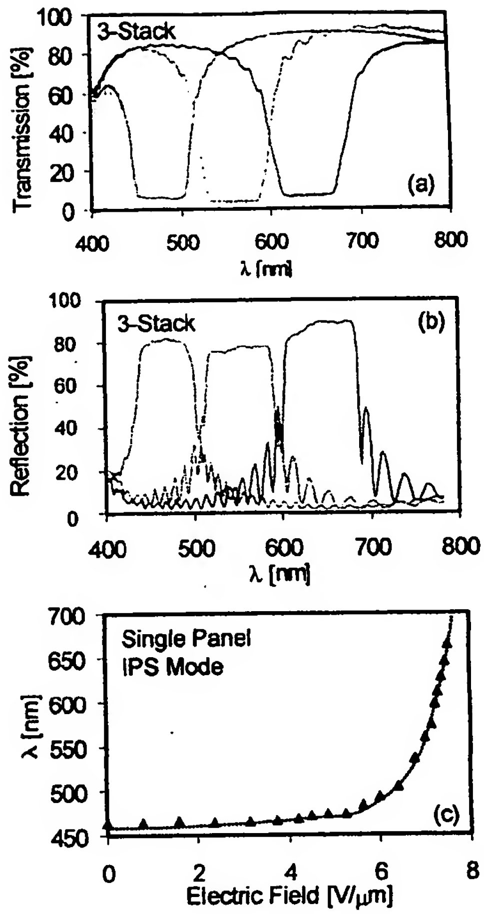

Figure 6: A CLC stacked device consisting of three panel pairs to reflect red, green and blue, shown in transmission (a) and reflection (b). A single panel CLC IPS device that nearly covers the entire spectral range (c).

Since the CLC solution can span the entire visible range with ~ 2 nm of , we believe that it is most suitable for the bruising application. We will follow two technical paths initially to find the appropriate solution. First we will pursue a stacked solution, similar to that illustrated in Figure 6(b) and experimentally evaluated in 7(a) and (b). The full spectral width of the reflection peak in Figure 6 (b) is large ($\Delta\lambda_{FWHM}$>100 nm). The spectral width is largely dictated by the birefringence of the CLC material (Δn). We will investigate materials with a low Δn to decrease the spectral bandwidth. For example, for a material with a Δn~0.05 we can expect spectral bandwidths on the order of $\Delta\lambda_{FWHM}$~30 nm for λ_B=600 nm, using the estimate that $\Delta\lambda_{FWHM} \sim \lambda_B \Delta n$. We could stack 10 panels to achieve full spectral coverage in the visible. The CLC materials do not have the scattering losses analogous to those observed with H-PDLC panels. We also do not expect to use the bistable mode of operation (focal conic) since it is not necessary for this application. We will therefore switch between the planar reflecting state and the transparent homeotropic state. We will also investigate the IPS mode single panel solution. This is an attractive approach since it only requires one panel and simplifies the engineering. The downside of the IPS CLC single panel technology is that the electrodes on the surface reduce the optical throughput (CLC does not respond above the electrode) and therefore reduces the overall reflection efficiency. To alleviate this problem we propose to offset transparent conducting electrodes on the top and bottom substrates and drive them with voltage signals out of phase. We believe this unique approach can lead to CLC switching over the entire panel and we will not suffer aperture losses. Another disadvantage is that the switching voltage is higher in the CLC IPS mode (electric field of 8 V/μm needed for spectral coverage) as compared to the conventional IPS mode. We will th refore bring our IPS electrodes clos r together (target 5 μm) so that maximum drive voltages would not xceed 40-50 volts. The proposed engineering of the CLC panels is challenging but we do not think it is insurmountable.

C.3.3 Deformed Helix Ferroelectric Liquid Crystals

A ferroelectric liquid crystal, or chiral smectic C phase (SmC^*), consists of layers of molecules. The thickness of the layers are less than one molecular length [*Yeh and Gu, 1999*]. As a result, the molecules must tilt at an angle with respect to the lay r normal. Because the tilt angle is fixed, the molecular orientation is confin d to a cone with a half apex angle of θ. The ferroelectric liquid crystal also has intrinsic chirality, much like the CLC and therefore has a pitch associated with it, and it has a dipole moment perpendicular to the long molecular axis (rather than parallel as in the case of CLCs). In ferroelectric switching, the molecules switch on the cone. We are proposing to use a deformed helix ferroelectric liquid crystal (DHFLC), first utilized in display applications [*Verhulst, et al., 1994*]. We propose a different mode of operation of the DHFLC. Rather than start with parallel boundary conditions as in displays [*Verhults, et al, 1994*], we will use homeotropic alignment at the surfaces (molecules aligned perpendicular to the surfaces). In this way, our panel provides a reflection, much like the CLC. Dynamic switching times for DHFLC are expected to be <500 μs.

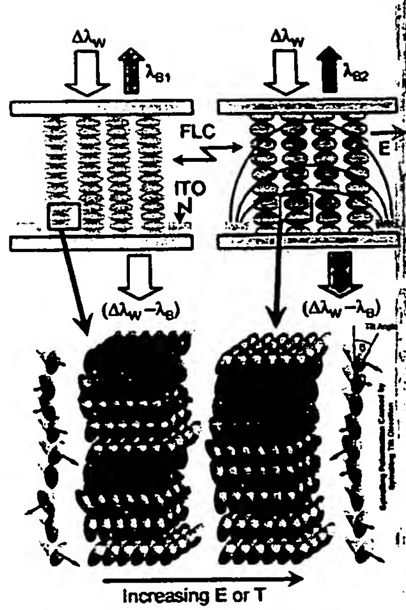

Figure 7: *The DHFLC modes of operations when subjected to an in-plane switching drive scheme, resulting in a red-shift. A red shift can also be obtained by heating the sample.*

The DHFLC is schematically presented in Figure 7. The pitch can be deformed using either an in-plane electric field or temperature. Upon application of an in-plane electric field, the helix deforms (elongates) and the reflection red-shifts. The electric field case shown in Figure 7 is the IPS mode of operation (also used for CLCs in Figure 5(c)). In order to prove the concept, we recently prepared a sample with homeotropic boundary conditions and subjected it to temperature increases. The data is presented in Figure 8 (a) and (b) for transmission and reflection, respectively. Since the refractive index of the material tested was small and the cone angle was around 30°, we titled the sample with respect to the incident light to increase the index perturbation with respect to the incoming light. We have shown in Figure 8 (c) that the DHFLC panel can cover the entire visible spectral range. Assuming linearity in the transition region in Figure 8(c), the tunability/resolution metric is $\Delta V/\Delta\lambda \sim 0.12$ °/nm.

The DHFLC is a wildcard technology in some sense. If it outperforms the H-PDLC and CLC technology, it could be used for both the conjunctiva and bruising application. We propose to study both IPS electrical switching and thermal switching for the DHFLC. Even though thermal switching may not be as attractive as electrical switching, it has been utilized in other thermal optical devices (*e.g.* for example in telecommunications). We will evaluate the use of a transparent resistive heater to see if thermal switching is fast enough. If the device can swing through the wavelengths in the visible spectral range on the order of hundreds of milliseconds, thermal addressing may be practical. We will also investigate the use of IPS DHFLC modes, which has the same disadvantages as those disclosed for the IPS CLC approach (*Section C.3.2*). We will therefore bring our IPS electrodes closer together (target 5 μm) to minimize aperture losses. The index modulation of the DHFLC is smaller than that for CLCs so we will evaluate materials with larger cone angles and higher refractive indices. The DHFLC is an attractive technology and we believe that we can push this technology forward to be useful for our applications outline in this proposal.

C.4 Proposed Research Plan

Our proposed research agenda is a genuine fusion of life science and engineering principles geared toward fabricating a biophontonics device that can satisfy needs of physicians. We are applying our engineering knowledge base and expertise to satisfy our goal to accurately measure hemoglobin in a non-invasive, fast, portable, and effectiv way, and to accurately determine th age of bruises. Our research plan is summarized in Figure 9.

Year 1: During the first year, Crawford will investigate the spectroscopic capability of the liquid crystal technology outlined in Section C3, advance the optical design, and optimize and improve the material and electro-optic performance. In parallel, Jay and Duffy will engage in the biological aspect of the conjunctiva, spectrometry and spectral imaging of the conjunctiva and bruises, and correlate the spectroscopic data to hemoglobin concentration (anemia) or hemoglobin degradation and aging (bruising). The two efforts will take place in parallel, with weekly meetings and graduate/medical student exchange between laboratories. Brown and Rhode Island Hospital are in close proximity (5 minute drive) making the logistics of meeting and collaborative work easy. In addition, we recruit students and interact with the *Women in Science and Engineering* (*WiSE*) and the student chapter of the *Biomedical Engineering* (*BME*) Society, we will hold an entrepreneurial workshop for students with an emphasis on the biophotonics industry, and our physician's seminar series will commence (see Section C.5).

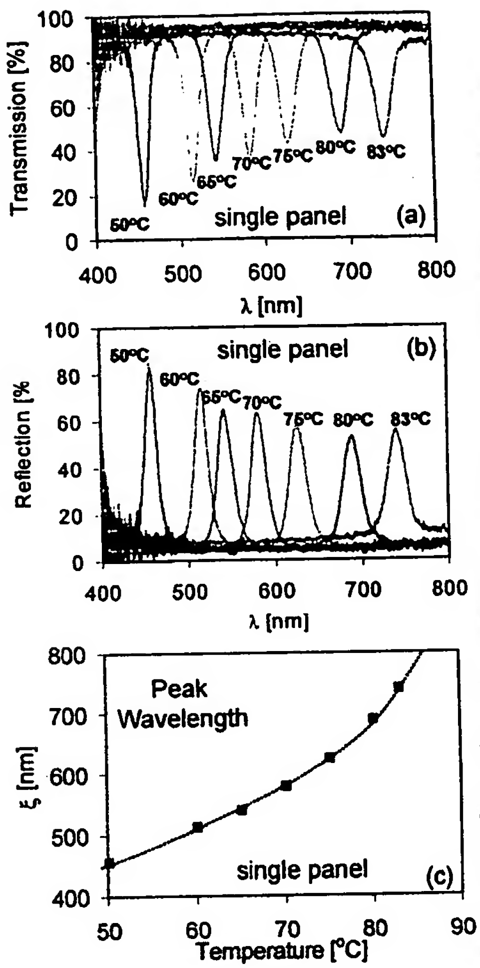

Figure 8: Spectral data of a DHFLC in transmission (a) reflection (b) as the temperature is changed, and tenability as function of temperature (c).

Crawford will be predominately focused on the spectroscopic features and electro-optic performance parameters of H-PDLCs, CLCs, and DHFLCs. We will study several metrics associated with each optical technology to ascertain its potential in the two applications (potential resolution, threshold and saturation voltages required for electrical addressing, dynamic response time, reflection efficiency, stackability, and spectral coverage). The spectroscopic application requires aggressive goals to be achieved that are not currently relevant to the display industry; most notably, being able to tune the reflection peak continuously over the visible spectrum. Using IPS addressing schemes in CLC and DHFLC, thermal addressing in DHFLC, tunability in H-PDLCs, and operating the DHFLC in the reflection mode is novel and is expected to significantly enhance the engineering knowledge base with the potential of other industries being able to capitalize on the results (e.g. displays and telecommunications).

Jay and Duffy will collect all available medical data on the conjunctiva and bruising and will focus on the physiology of the conjunctiva and the bruising process. With the cooperation of a graduate student from *Brown University*, they will perform controlled spectroscopic experiments on the conjunctiva and bruising. Since they have existing research in this area, all necessary approvals will be in place for the study. Jay will take spectra of the human beings conjunctiva using a conventional spectrometer and will begin to correlate this measurement to the CBC test. In addition, Jay will investigate the spatial variation of the spectral signature of the conjunctiva. In the preliminary investigation of bruised tissue, Duffy we will recruit volunteers with bruises of known force and duration and measure their spectroscopic signature with a conventional spectrometer. Additionally, she will study patients with bruises of known etiology and duration with the spectroscope. Duffy will also inflict bruises on volunteers with a standard force in similar locations and follow their course with digital photography alongside a standard color wheel during their visible lives and then document their non visible duration with UV light. In addition we will be assessing bruises in pediatric patients and assessing location, mechanism and timing of the bruises as well as parents' and patients' recall of th timing and circumstances. Crawford and th ngineering stud nts will work closely with Jay, Duffy and their students to analyze the spectroscopic data and begin the correlation process.

Year 2: During year 2, we will continue with our aggressive education program by integrating our findings into the Biophonics course taught by Crawford, continue with our physician s minar series in the Department of Emergency Medicine, and begin to interact with *Slater Center for Biotechnology*. Although the students and PIs have been closely collaborating in year 1, year 2 will see the convergence of the electro-optical technology and the biomedical results. Based on a selection criteria, spectral coverage, threshold and saturation voltage, reflection efficiency and dynamic response, the optimal technologies will be selected that best satisfy the proposed applications. We will also push the spectral coverage of the technology out to the near infrared, possible with all technologies, for the bruising application.

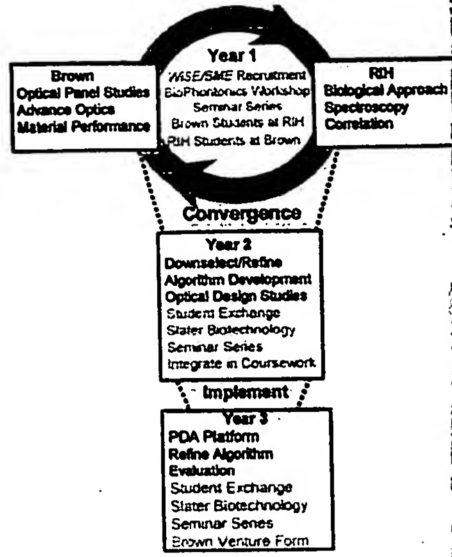

***Figure 9:** Research plan flowchart.*

Crawford will continue to optimize the selected electro-optical technologies and begin building a bench-top prototype. Crawford will investigate the system in both transmission and reflection modes of operation and see which approach best enables one to reconstruct the spectral signature of tissue being probed. It is anticipated that reflection will be a better option since the contrast of the system will be much higher. When the transmission mode is utilized, both in-band leakage (seen in Figures 4, 6 & 8) and scattering will be an issue. Figure 10 shows a schematic illustration of a reflective mode configuration. We anticipate that our collection cone (field of view) with be small since the areas we wish to probe will be on the order of millimeters and the device will be in close proximity to the patient. The conjunctiva application we expect to probe a 1-2 mm area and for bruising we expect to probe a 5 mm area. Since we have a small field of view, we do not expect that sophisticated lens arrays will be required on the input or output of the device. In addition, the Bragg shift will be very small for rays coming in at different angles into the input of the system since the collection cone is small. If this does present a problem, it can certainly be corrected in the software. There are several questions that need to be addressed at this point. What will be the light source and can it also do spectral imaging and how useful will it be for the disclosed applications? We have two options with the light source and we will investigate both pathways. The first option is to use a standard broadband light source and the second option is to use a gray scale card (next to the image) so that an algorithm can be created to normalize the light intensity. In addition, we will investigate if incident polarized light can reduce reflections from the conjuctiva/bruise to enhance optical contrast. We will investigate both approaches in the context on which solution provides the best accuracy and which is preferred by potential users of the device. For both cases, we will investigate spectral imaging on the pixel level of the CCD. With high resolution CCDs available, we expect that we may capture the spectra of a single blood vessel in the conjunctiva. Crawford and Jay will investigate pixel averaging techniques and spectral imaging techniques to see if there is added value if a single blood vessel can be imaged. For bruising applications, spectral imaging may also be of benefit. Crawford and Duffy will perform pixel averaging and spectral imaging techniques on bruises.

Year 2 will also be a cornerstone for developing a spectroscopic model and algorithm for both applications so that the experimental spectrum can be fitted to obtain quantitative information (e.g. hemoglobin concentration). Since the conjunctiva is relatively transparent in the visible and the blood vessels are in close proximity to the surface, scattering and absorption effects are negligible, making this model relatively straight forward. In our application, we measure the reflectance spectra so that we can extract the concentrations of various chromophores of interest (*e.g.* oxy- and deoxy-hemoglobin). We propose to construct the simplest model based on the Beer-Lambert law (since the conjunctiva is transparent and blood vessels are close to the surface) that relates th overall attenuation of the conjunctiva, $-ln(I/I_o)$, to its absorption coefficient, where I is the light intensity.

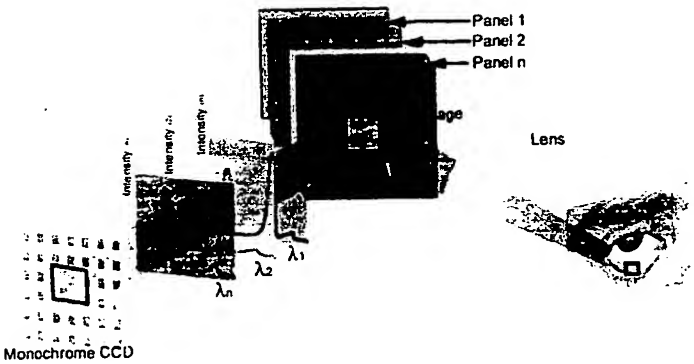

Figure 10: Schematic illustration of a three panel stack operating in reflection.

There is currently no objective standard for assessing bruises in living patients. Color alone is inadequate for dating bruises because skin pigment, skin type and depth and involvement of other tissues impact the visibl spectrum [*Sprigle, et al., 2002*]. Pathological examination, of bruised tissue sections are used in forensic laboratories and the ages of bruises are determined by the breakdown of hemoglobin in the tissue. Translating this objective process to living bruised skin is the challenge. Spectrophotometry has been used in dermatology research to analyze skin pigment and differentiate pathologic lesions from benign lesions based on color [*Dawson, et al., 1980*]. Modeling a bruise is a much more formidable task since, unlike the conjunctiva, it represents a complex inhomogeneous multi-layered highly scattering and absorbing medium. We plan to utilize the model recently proposed by Meglinski and Matcher (2003) which models the reflectance spectra of skin using Monte-Carlo techniques. The model takes into account variations in the spatial distribution of blood, level of blood oxygen saturation, volume fraction of water and chromaphore content [*Meglinski and Matcher, 2003*]. The model is one of the most sophisticated models available and assumes that the skin is divided into seven layers and given the inhomogeneous distribution of blood vessels in the skin, the dermis is divided into four sublayers each with its own blood volumes. The model is based on modeling normal skin, so we will adapt it to model bruised skin. The trauma of a bruise ruptures blood vessels in the skin and therefore we expect that the spectral signature of a bruise can also be predicted with this model. We want to investigate if we can extract or measure hemoglobin breakdown in the skin and correlate this to the age of the bruise. This is used in forensics on cadavers to obtain evidence, but it is not clear if it can be used as a standard in living patents. Duffy will investigate this issue. Crawford and Duffy will develop this adaption of the *Meglinski and Matcher* model for bruised skin. Crawford has experience with Monte Carlo Simulations in his liquid crystal work [*Amimori, et al., 2003*]. Another interesting aspect about the skin/bruise model is that more information can be obtained if the spectral range is extended into the near infrared region (to 1000 nm). Although this presents a formidable engineering challenge, all of the proposed technologies can in principle be designed to work at this wavelength. It will be a subject of year 2 to also push the reflection capability of the selected optical devices out to the near infrared and evaluate light sources that can satisfy this broader wavelength range.

Year 3: During year 3, the integration of all technology and medical science will take place. The attractive feature about our proposed device is that it can potentially be very small and portable, and inexpensive. We strongly believe that if this device can be packaged in a small container (<200 cm^3) and if it can be integrated with a PDA (most physicians now use PDA), it will see wide spread usage in the medical community. During this final year, we will focus system requirements, packaging, and integration with a PDA platform. We will continue our physician seminar series and interactions with *Slater*, and in addition, we will present our work at the *Brown Venture Forum* to move our technology to commercialization. We will also finish up any optimization of our electro-optic panels and further refine our model if necessary. In the spirit of the NSF announcement, we will also evaluate our technology in a clinical setting at *Rhode Island Hospital* at the culmination of the grant.

Many of today's portable digital assistants (PDA) run simpler versions of the common Microsoft Windows operating system known as PocketPC. The USB interface has become a standard component in today's PCs. The majority of peripherals sold today (scanners, digital cameras, printers, etc.) are interfaced to a PC with a USB connection. Using this USB connection, the data can then be transmitted to a PDA. In order to perform this transfer, we will dev lop a simple program that can interpret the data sent from the CCD into a format, which can be read by the PDA. This should be relatively straight forward since software currently exists to transform CCD data into images on any digital camera as well as software that can translate data from a USB w bcam into an image stream. The output data from our system

could b processed by this software to form a tagged image file format (TIF) image, or it could b sent to the PDA as data valu s for storag and manipulation using *Excel*, *Matlab*, or a similar program.

Th following is a brief overview of the op ration of our proposed system. Analog imag data will be collected by the CCD, which will hav to be driven by a complex clocking scheme in order to properly time the acquisition and handoff of the data. The collected data will then be passed along to an analog signal processing circuit where the data is amplified and filtered in order to be properly converted into a digital signal. This analog to digital conversion will transform the analog data into 16-bit serial data, which can be read by a USB transceiver. The USB transceiver will be set up to receive the serial bit stream from the analog to digital converters (ADCs) and transmit the data to the PDA. This system could also be used with a PC if portability is not an issue. The CCD array usually needs multiple levels of voltage. The ADC and op-amps also need positive and negative supply voltages. The ±15V input from the supply is converted by the SVN into the necessary voltages to supply the power and biasing signals to the components as needed. The CCD requires complex timing schemes for data readout, image acquisition setup, and data transfer. This block will provide the necessary clocking and signal conditioning required for this task. The CCD will act as the input source for the system capturing the desired spectral information and pass it to the analog signal-processing block. In addition to driving and capturing data off of the CCD, we will also need to drive the electro-optic panels. We will leverage off of a current circuit designed in our laboratory for display applications (battery, inverter, and transformer combination) to electrically address the panels (output ±100 V). We can perform all of the packaging of our optics and electronics using our rapid prototype facility located in the new engineering building at *Brown University*.

Engineering Outcomes: We have proposed to apply many optical and materials engineering principles to advance the engineering knowledge base as an outcome of our work. We have utilized materials that have been predominately used in the display industry to create a biophotonics device with spectral imaging capabilities. Several new engineering outcomes are possible in this study in addition to the applications described in this proposal. First, we will use IPS switching in CLC and FLCs which is a novel way to drive these devices. Second, we leverage off of current know-how in electro-optics to create devices with spectral imaging capability – A new application for this technology. Third, we have proposed a new configuration for DHFLCs to capitalize on their reflection properties rather than changes in average birefringence, and we have also proposed a way and proof of concept data on how to thermally address the DHFLC devices. Fourth, we are operating the H-PDLC in a tunable mode, rather than its typical binary operation. These new developments may have broader potential in applications outside the scope of this proposal; namely display and telecommunications devices. In addition, we are working on the interface between medicine and engineering, where technologies, concepts, and models converge to enable new devices for the benefit of humanity.

C.5 Broader Impacts / Educational Plan

The PIs are genuinely committed to integrating education and research. The educational component is also intended to prepare students to participate in the growing field of biophotonics and to better train students in the integration of basic engineering and life sciences principles in solving multidisciplinary biomedical problems that can ultimately benefit society. Since there is a tremendous need for highly trained students in the biophotonics sector, we have prepared an aggressive integrated education program for all levels.

C.5.1 Education Outreach

We plan to develop a Web page that can be used by middle and high school students to learn about anemia and bruising, and discuss how spectroscopy can be used to accurately measure levels of hemoglobin in both the conjunctiva and in bruised tissue. One aspect of the Web page will be a digital gallery of images where visitors can perform on-line virtual spectroscopy experiments (*e.g.* look at a digital image and compare it to a corresponding spectrum). The module will enable students to learn about the visible spectrum, as w ll as gain a deep appreciation of the valu of analytical tools in science and medicin . In addition, we will also create th virtual doctor modul that will nabl stud nts to us

on-lin virtual instrumentation to measure hemoglobin in conjunctiva samples and to age bruises so th y make the connection betwe n the spectroscopic technique and its potential clinical use.

Th NSF MRSEC at *Brown University* has an xceptionally strong education outreach program for local students and teach rs. They frequ ntly tour our laboratories and faciliti s to see first hand what it means to be a scientist or an engineer. The biomedical device proposed here will be put on the facilities tour menu so students, teachers, and the community can also benefit and learn more about what faculty and physicians are working on in the community. Since this is a non-invasive technique, we can demonstrate how it works during the tour. *Crawford* also specializes in outreach for troubled teens, with cooperation with the *Boys & Girls Club of Pawtucket*, *The Rhode Island Training School* for incarcerated juveniles, The *Urban League Bridge School* for expelled high school students, and the *Rhode Island School of the Deaf*, all of which will benefit from the web site or on-site tours.

C.5.2 New Biomedical Engineering Program/Courses at Brown University

Brown University is developing a new Center for Biomedical Engineering that is sponsored jointly by the *Division of Engineering* and the *Division of Biology and Medicine*. This effort has resulted in the stablishment of a newly reorganized undergraduate concentration in bioengineering approved in the fall of 1999 (the first four year class graduated in 2003), and an award from the *Whitaker Foundation* to assist with start-up financing for new faculty positions and the development of a joint Ph.D. program. There are a number of biomedical engineering courses now available at *Brown University* for students to choose from. Crawford is developing and will also teach a new course in the Fall of 2004, entitled *Biophotonics* (Engineering 292). The applications and technology discussed in this proposal are highly synergetic with the planned course syllabus and therefore will be integrated into the class. The proposal and the course are a perfect match! More can be found at www.engin.brown.edu/undergrad/bioeng/.

C.5.3 Biomedical Engineering Society

The Brown *Biomedical Engineering Society* (*BMS*) is a student chapter (established in 2001) of the *Biomedical Engineering Society*. The mission of the *BMS* is to inform the entire community of advancements and accomplishments pertaining to biomedical engineering. They also provide resources to, organize events for, and promote collaboration between students of biomedical engineering at *Brown University*. There are several ways in which we will cooperate with *BME* (see support letter). *The BME* can help us identify interested students concentrating in biomedical engineering to work on the project. If our proposal is successful, we will immediately apply for additional funding to support undergraduate students through the *NSF*'s Research for Undergraduates (*REU*) Program. The *BME* also organizes laboratory tours at *Brown University* to show students the cutting edge research being performed on campus, so we can also capitalize on this activity to show students our research progress. In addition, the *BME* largely interacts with its student members through their website so we can utilize the BME website as a vehicle to advertise our research program, new course offerings on *Biophotonics*, and our entrepreneurship event to insure our efforts have a strong following. More information can be found on our website: www.brown.edu/Students/Biomedical_Engineering_Society.

C.5.4 Entrepreneurship/Commercialization Workshop

Crawford has recently been awarded a small $4,000 grant from the *International Society for Optical Engineering* (*SPIE*) to fund a workshop for students on optics and entrepreneurship in the Fall of 2004. Due to the explosive growth in biophotonics in the last few years, a significant portion of the workshop will be dedicated to biophotonic start-up activities in the Northeast. The goal of the workshop is to entice students to think about alternative career options – *i.e.* high technology entrepreneurship. The workshop will involve speakers from venture capital firms, intellectual property firms, and angel investor groups, in addition to case studies focused on biotech companies and small start-ups that are successful at winning SBIR/STTR grants. Crawford organized a general entrepreneurship workshop for graduate students in 2003 entitled *Creating value out of Basic Research*, which was attended by >100 graduate students.

C.5.5 Physician Seminars

We propose to make a strong connection with clinical needs of physicians at *Rhode Island Hospital* and surrounding hospitals. Our current biomedical ngineering seminars focus on current r s arch of faculty

and company scientists. Rather than add more research seminars on biophotonics, w propose to hold 3-4 seminars per y ar that will host a physician to come in and discuss his/her needs to the students. For example, th Jay and Duffy applications and needs described in this proposal would be a wonderful starting point. The physician will com in and d scribe the clinical problem and/or 'bottleneck' in his/work work (fast and reliable way to measure hemoglobin or an accurate way to age bruises) and ncourag students to discuss solutions in an open forum. We believe that this will ncourag students to use th ir backgrounds to critically think about new applications that can satisfy current needs of the medical community. The physician seminar series would expand beyond Emergency Medicine into other Medical School venues such as Surgery and Radiology for example.

C.5.6 Commercialization

Although commercialization is probably the most appropriate way to convert academic research results and developments into societal benefit, it is a rare event. We feel that our proposed research will have significant application potential to the medical community and therefore the health of people. In addition to dissemination of our results through the normal routes that academicians often pursue (publications and conference presentations), we will parallel these efforts with a close relationship to the business community in Rhode Island using two different 'vehicles'; (1) the *Brown Venture Forum* and (2) *Slater Center for Biotechnology* (see letters of support). We proposed to capitalize on the extensive network capability of these two organizations to find interested third parties to develop our technology. We believe that the *Brown Venture Forum* can serve as an interface to local industry to help identify the appropriate people and resources to assist in commercializing our biophotonics device so that it can more quickly benefit humanity. The *Brown Venture Forum* usually has more than 100 attendees during a given monthly meeting, comprised of a diverse group of local business professionals, state government policy makers, venture capitalists, angel investors, intellectual property attorneys, scientists, engineers, seasoned entrepreneurs, and many others interested in high technology and entrepreneurship in Rhode Island. In Year 3, we will present our findings at a *Brown Venture Forum* meeting dedicated to biophontoics. The *Slater Center for Biotechnology* will also be a valuable resource for commercialization since it is a vehicle for entrepreneurs and small companies to acquire start-up capital for new ideas. We will closely cooperate with *Slater* over the duration of the grant to find interested third parties who can assist us in moving our work towards commercialization.

C.5.7 Diversity: Outreach to Minorities and Woman

The PIs are genuinely committed to diversity by attracting and retaining women and minorities in science, engineering and medicine. The Division of Engineering at *Brown University* has an outstanding record of accomplishment in this area, with more than 30% of its freshman undergraduate engineering class being women, and the retention percentage for women and minorities in our undergraduate program being comparable to any other demographic group. Additionally, one of the PI's on the proposal is a woman and will serve as a role model for students engaged in the project. Biology and Medicine traditionally have more women graduate students so we expect that the user group from this area will increase th use of this equipment by women. A second area where this effort will become important will be the Research Experiences for Undergraduates (*REU*) program within the *NSF MRSEC* on Micro- and Nano-Mechanics at *Brown University*. The *REU* program has created genuine relationships with three historically black universities: *Hampton University, North Carolina Agriculture and Technical State University*, and *Florida A&M University*. The *REU* program in 2001 included seven minority students from these three universities, four of which were women, and in 2002 and 2003 there were ten and eight participants, respectively. One minority student from the 2002 REU experience is currently in our graduate program. The MRSEC plan requires REU students to gain a working knowledge of at least three experimental programs, and our efforts in biophotonics will be in the list of possibilities. Additionally, *Brown University* has active chapters of *Women in Science and Engineering* (*WiSE*) and the *National Society of Black Engineers* (*NSBE*). *WiSE* also supports a *Women of Color Program* that serves as a liaison to other campus organizations, such as *NSBE* and the *New Scientists Program* for minority students. The faculty strongly support *WiSE* and *NSBE* through presentations and laboratory tours. Crawford co-organized an event with Katharine Wilson (coordinator of *WiSE*) in the Spring of 2002 and 2003 entitled *Empowering your Future*, which brought middle school girls and parents to campus for on day to engage in science and engineering activities and workshops, and to tour the research facilities. Th PIs are all committed to div rsity issues and with the close coop ration with these campus-based

organizations (see attached letter of support), w believ that w will be successful in attracting some of the best and brightest students to our research laboratories, as well as disseminating the information about biophotonics to large women and minority populations who have a general interest in science, engineering, and medicine.

C.5.8 Broader Impact of Proposed Device to Society

A device that can quickly, accurately, and portably measure hemoglobin has many medical applications and benefits, such as in routine physical examinations, in emergency rooms, for emergency rescue professionals, during surgery for in-situ measurement of hemoglobin to check for bleeding, home health care for the chronically ill and aging population, in developing countries where anemia is prevalent and and medicine is practiced in the field, military medical units, mass casualty situations and triage units, and specialists who deal with anemia on a regular basis (*e.g.* oncology, pediatrics, obstetrics, gynecology, anesthesiology, infectious disease, gastroenterology, cardiology, nephrology, geriatrics, nutrition, and urology). Anemia occurs more frequently among the elderly, and its prevalence is expected to increase as babyboomers become senior citizens. Since anemia is a consequence of many more serious diseases, early detection, diagnosis and treatment of the more serious disease will greatly benefit society and potentially reduce health care costs. Not only is anemia a consequence of disease, it may also be induced by the treatment of the disease itself, such as patents with cancer, HIV/AIDS, and hepatitis C. With respect to the bruising application, we believe the device will significantly benefit society because decisions with grave consequences are based on a physician's opinion in abuse cases. We also believe that our proposed portable spectroscopic imaging device can be extremely useful in other applications, including dermatology, forensics, and dentistry.

C.6 Results – Prior NSF Support

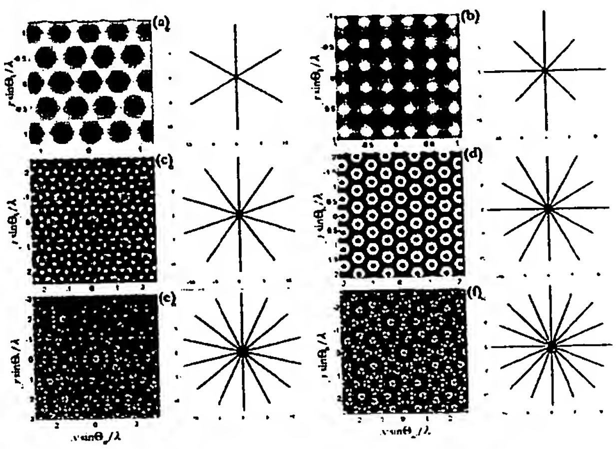

Figure 11: The irradiance profiles (left) and normalized reciprocal wave vectors (right) resulting from the interference of N-beams with the same polar angle and equally distributed along the azimuth. (a) through (f) correspond to N = 3 through 8, respectively.

<u>Crawford (ECS 0322878)</u> *"Investigations of Switchable Mesoscale Lattices for Photonic Applications"* This project focuses on discovery and application of two- and three-dimensionally structured liquid crystal polymer dispersions for the creation of electrically switchable mesoscale lattices targeted at photonic crystal (PhC) and diffractive optical applications. Holographic-lithography at 351 nm or 532 nm is being investigated to generate optical lattices that permanently capture the spatial segregation of liquid crystal droplets in a 2D or 3D lattices through a photo-assisted diffusion and phase-separation. We are creating many mesoscale lattice configurations with this technique, such as the diamond lattice, superimposed lattices, quasilattices, and superlattices. The project theme is discovery and application of novel mesoscale switchable lattices and their potential application in photonic devices (*e.g.* lasing, waveguides, strain-gauges). Examples of irradiance profiles are shown in Figure 11 demonstrating the wide variety of possible symmetries that can be captured in liquid crystal polymer composites using N-beam exposures. The program began in September 2003 and has resulted in one invited publication to Optical Engineering [*Escuti and Crawford, 2004-a*] and one conference proceeding [*Escuti and Crawford, 2004-b*]. <u>Crawford's</u> CAREER Award (1999-2004: DMR 98-75427) has resulted in > 40 publications acknowledging the award.